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The effects, costs and savings of neonatal screening for Cystic Fibrosis

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The goal of neonatal screening for Cystic Fibrosis is to start therapeutic interventions as early in life as possible. By early intervention, organ damage can be prevented or postponed for as long as possible. The potential to inform parents about genetic risks before a next pregnancy is another benefit of newborn screening for CF. As a result, the prevalence of offspring born with CF will be reduced as compared with a situation without CF screening.
Currently, neonatal screening for CF is implemented in several countries. In The Netherlands however, introduction of neonatal screening for CF is still under debate.
Aim A review of the effects, costs and savings of newborn screening for CF in The Netherlands to provide information in the decision process of including neonatal screening for CF in the current newborn screening program.
Methods The required information was collected by the use of clinical information, a systematic review of the literature and expert opinions. The costs of screening and accompanying diagnostic procedures were estimated in circumstances with screening and circumstances without screening. Also, the savings generated by parents with a child with CF deciding not to have another child, were included. Sensitivity analyses, varying the values of several assumptions, are currently executed.
Results The study will be completed by March 2005 and data can be presented at the conference.

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Validation of a new line probe assay for the amplification and simultaneous detection of 21 Italian *CFTR* mutations

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The performance of INNO-LiPA *CFTR* Italian Regional for the detection of 21 Italian *CFTR* mutations and their wild-type sequences was validated in-house. A total of 85 anonymous whole blood samples, originating from different countries, was amplified, 84 of which where analyzed with the regional strip.
For these samples a concordance of 96.4% (81/84; 95% CI [89.9%; 99.3%]) with conventional genotyping methods was observed after initial testing, with 100% (84/84; 95% CI [95.7%; 100%]) concordance after discrepancy testing of three samples. Upon initial testing, INNO-LiPA *CFTR* Italian Regional detected mutation S549R A→C (tested three times) in two samples, and mutation G1244E (tested three times) in another sample. Sequencing of all three samples confirmed the result obtained with INNO-LiPA *CFTR* Italian Regional.
Development of the assay has aimed at avoiding reactivity with other than the specified mutations or polymorphisms in the *CFTR* gene. The eight different mutations/polymorphisms encountered in this study did not show any cross-reactivity with the probes present on the strip.
DNA extracted from ten buccal brush samples and twenty dried blood spots from healthy blood donors was also successfully genotyped.
In conclusion, this study showed that the INNO-LiPA *CFTR* Italian Regional is a reliable and accurate test for the detection of 21 Italian CF-related mutations in the *CFTR* gene region.

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Sweat testing equipment compared: the Nanoduct versus the Macroduct

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The Macroduct system and the semi-quantitative measurement of sweat conductivity is generally considered as a reliable screening instrument for sweat testing[1]. However, in small infants the Macroduct often fails to induce sufficient amounts of sweat for analysis. According to the manufacturer the Nanoduct can perform a reliable analysis of electrolytes in sweat in minimally 3 µl sweat.
Aim. To assess the performance of the Nanoduct for sweat testing.
Patients and methods. Sweat tests by means of the Macroduct and the Nanoduct were carried out simultaneously in 13 patients with CF, age 1.6 – 20.2 yrs, and in 22 controls, age 6 days-12.7 yrs. Then chloride concentrations of the collected sweat samples in the Macroduct coil system were determined according to standard procedures. Sweat tests with semi-quantitative values of ≥ 50 were considered positive. Bivariate Pearson's *r* was calculated for correlations.
Results. The Nanoduct was successful at the first attempt in all subjects, while the Macroduct had to be repeated in 7 (20%). The results of the Nanoduct highly correlated (r=0,969) with the quantitative chemical analyses. For both the Macroduct and the Nanoduct a sensitivity of 100% was observed. Positive predictive values were 100% for the Nanoduct, and 75% for the Macroduct.
Conclusion. The Nanoduct seems to be a reliable instrument for sweat testing. It's use might be considered in excluding or confirming CF in newborns with a positive screening test for CF.
Reference. 1. Le Grys VA. J Pediatrics 1996, 892-7.

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Guidelines for announcing the diagnosis of cystic fibrosis after neonatal screening

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Introduction: The French CF Association "Vaincre la Mucoviscidose" has for many years promoted neonatal screening. Decided en 2002 by the French Health Authorities, every region in France has implemented CF neonatal screening under the responsibility of the screening program Association (AFDPHE). Screened babies are referred to one of the 30 pediatric accredited CF centre. The conditions of disclosure of the diagnostic and the initial contact between the CF centre and the parents are determinant to establish a confident relationship involving parents as real partners of care.
Aims: A working group met to discuss optimal announcement procedures for a disease like CF, in this particular pre-symptomatic context, in order to minimize as much as possible parental stress, to obtain the best quality of care and to avoid any perturbation in the child's emotional development and the family stability.
Methods: After a large literature search, a working group (7 paediatricians, 1 specialized nurse, 1 physiotherapist, 1 social worker, 2 psychologists and 2 parents) elaborated guidelines. The document has been validated by paediatricians from the medical council of "Vaincre la Mucoviscidose" and by 14 parents. This brochure was published and addressed to every CF team.
Results: The guidelines are divided in five themes: who should announce; with whom can the announcement be made; to whom should the announcement be made; how must the announcement be made; what should be announced. Guidelines are adapted to the results of the tests: IRT, genetic testing, sweat test.
Conclusions: Beyond valorising the results of this work, the next two steps will be to set up information tools for parents and families, and to evaluate the impact of these guidelines upon parents and health care providers.